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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,351	KORNECKI ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/21/10 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 7/21/10 is acknowledged. Claims 1-17, 19-20 and 26-31 are cancelled. Claims 18 and 22 are amended. Claims 18 and 21-25 are pending in this application and under examination in this office action.

3. Applicant's arguments filed on 7/21/10 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

4. The rejection of claims 18 and 21-25 under 35 U.S.C. 102(b) as being anticipated by GenBank accession number AA101561, October 1996.

Claim Rejections/Objections Maintained

In view of the amendment filed on 7/21/10, the following rejections are maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 21 stands rejected under 35 U.S.C. 102(b) as being anticipated by GenBank accession number AA101561, October 1996. The rejection is maintained for the reasons made of the record and the reasons set forth below.

Claim 21 is drawn to a DNA oligomer consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO:1, nucleotides 16-912 of SEQ ID NO:1, nucleotides 97-912 of SEQ ID NO:1 or a nucleotide sequence complementary thereto.

On p. 5 of the response, Applicant argues that the GenBank reference only discloses a single compound containing 415 nucleotides and does not disclose an oligomer having a length of 1822 nucleotides, an oligomer having a length of 897 nucleotides or an oligomer having a length of 816 nucleotides as recited in claims 18 and 22. Applicant argues that SEQ ID NO:1 is only 74.5% identical to SEQ ID NO:2, which is 99.2% identical to the molecule in the GenBank reference. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the DNA molecule recited in claim 21 encompasses fragments within SEQ ID NO:1, nucleotides 16-912 of SEQ ID NO:1 and nucleotides 97-912 of SEQ ID NO:1, or a nucleotide sequence complementary thereto because of the recitation "a

nucleotide sequence…". As previously made of record, the DNA oligomers recited in instant claim 21 encompasses any fragments with different lengths derived from the sequence of SEQ ID NO:1, nucleotides 16-912 or 97-912 of SEQ ID NO:1 or a nucleotide sequence complementary thereto. Thus, a DNA with a short sequence derived from SEQ ID NO:1, nucleotides 16-912 or 97-912 of SEQ ID NO:1 or a nucleotide sequence complementary thereto meets the limitation of "a nucleotide sequence …. of SEQ ID NO:1, nucleotides 16-912 or 97-912 of SEQ ID NO:1 or a nucleotide sequence complementary thereto". The DNA molecule of AA101561 is 99.2% identical to the sequence of the instant SEQ ID NO:2 over a region of 377 bases and the instant SEQ ID NO:2 is 74.5% identical to the whole molecule of instant SEQ ID NO:1 and with 99.1% local similarity. Thus, the DNA fragment (oligomers) of AA101561 meets the limitation "a DNA oligomer consisting of "a" nucleotide sequence (fragments) of SEQ ID NO:1, nucleotides 16-912 or 97-912 of SEQ ID NO:1" as recited in instant claim 21. Accordingly, the rejection of claim 21 under 35 U.S.C. 102(b) for being anticipated by GenBank accession number AA101561 (October 1996) is maintained.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 7/21/10.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18 and 21-25 are rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter.

Claims 18 and 21-25, as written, do not sufficiently distinguish over DNAs that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 10 of specification. See MPEP 2105.

Claim Rejections - 35 USC § 101

7. Claims 18 and 21-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966):

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

The specification only describes

"a nucleic acid molecule which encodes a human platelet F11 receptor is the molecule having the nucleotide sequence as shown in SEQ ID NO:1. Nucleotides 16-96 of SEQ ID NO:1 represent a signal sequence, and nucleotides 97-912 represent the mature protein (nucleotides 16-912 thus represent the F11 receptor with its signal sequence). Nucleotides 16-18 are an ATG start codon, and nucleotides 913-915 are a stop codon. The amino acid sequence encoded by this nucleotide sequence is shown in SEQ ID NO:3" on p. 28-29 of the specification.

However, the specification fails to provide any objective evidence of any activity for the claimed isolated DNA as recited in the claims 18, 21, 22. The rest of the claims depend from claims 18, 21 and 22. Although the specification describes assays to detect a human platelet F11 receptor in a sample on p. 28-30, the specification fails to demonstrate that the isolated DNA oligomer capable of binding the nucleotide sequences recited instant claims 18, 21 and 22 will predictably function as a human platelet F11 receptor(SEQ ID NO:3). The claimed polynucleotides encompass nucleotides encoding structurally and functionally undefined amino acid residues or encoding amino acid sequences with no function. In addition, although Applicant may be predictably to detect the transcripts of the isolated DNA oligomer in different tissues, Applicant fails to provide a nexus between the real function of the isolated DNA oligomer with any function of human platelet F11 receptor (SEQ ID NO:3). The art recognizes that expression of a particular nucleic acid specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. There are many steps/mechanisms to regulate gene transcription and protein expression. They include transcriptional regulation, translational regulation and post-translational regulation. For example, P53, a marker associated with tumor associated antigens, has been shown to have no consistent expressional levels of protein and mRNA in blast

cells from patients who are suffering from acute myelogenous leukemia but have no mutation in the p53 gene (Fu et al. EMBO Journal, 1996, Vol. 15, pp. 4392-4401). The detection of mRNA levels does not correspond to equivalent expression levels of protein and thus can not be used as a predictive marker for a disease. Furthermore, Applicant fails to disclose any diseases or conditions known to be associated with or affected by the claimed DNA oligomer. Merely listing a number of possibilities is not sufficient to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the encoded protein is involved. Thus, further research is required to verify whether the claimed DNA oligomers function as a human platelet F11 receptor or identify a disease for which they could be used, or a disease for which its presence would be diagnostic. Applicant thus does not identify or confirm a "real world" context of use; clearly further research would be required to identify a disease or function associated with these polypeptides and thus endow these polypeptides with a utility. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. See also the Revised Interim Utility Guidelines available at www.uspto.gov.

The claimed invention also lacks a well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Although Applicant describes assays for human platelet F11 receptor to detect the

claimed DNA oligomers, no domain structures that would identify the claimed DNA oligomers with limited homology to SEQ ID NO:1, nucleotides 16-912 or 97-912 of SEQ ID NO:1 are shown. Evidence based on protein or polynucleotide sequence homology does not alone permit extrapolation to biological function or use of an isolated DNA or amino acid sequence. Bowie et al. teach that a prediction of protein structure and function based on sequence homology data is problematic because the function of protein is complex. Although an amino acid sequence could be used to predict a three-dimensional structure and function of a protein, the prediction based on computational analyses only provides information for further functional characterization/research to reveal a real function of a gene (col 1, p. 1306, Bowie et al. Science, 1990, 257:1306-1310).

Comparative sequence analyses for functional prediction of a protein have been shown to be prone to errors. Although sequencing techniques have been highly automated and accurate and genes/sequences have been annotated, the quality of sequences deposited in the public database is still imperfect especially for protein function (p. 398, cols 1-2, Bork. Genome Research, 2000,10:398-400). Several factors affecting the accuracy of gene annotation and prediction of protein function include alternative splicing and post-translational modification. Alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at the protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). In addition, most features predicted with an

accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 paragraphs bridging cols 2 and 3). The reference cautions that although the comparative sequence analyses seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly (p. 400, para bridging cols 1 and 2). For example, Scott et al. teach that a functional prediction of pendrin, a gene responsible for Pendred syndrome, based on sequence homology is problematic (Nature Genetics, 1999, 21:440-443). Based on sequence similarity data, Scott et al. postulated that pendrin could function as a sulfate transporter protein based on its sequence having 29% identity to the rat sulfate-anion transporter, 32% similarity to the human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter. However, further functional characterization of pendrin showed that pendrin functioned as a transporter of chloride and iodide. Scott et al. emphasized that even the database searches reveal significant homology to proteins with known function, a further characterization of gene function is important to confirm/reveal the real function of a gene (page 411, 1st column, 4th paragraph).

Furthermore, the art recognizes that while many amino acid or nucleotide substitutions are possible in any given protein, the position of where such amino acid or nucleotide substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the

relationship of three dimensional structure and function of the protein (col 2, p. 1306, Bowie et al. Science, 1990, 247:1306-1310). It has been shown that a single amino acid change can alter the function of a protein. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 111:2129-2138, 1990). It has also been shown that different homologs of receptors even binding to the same ligand may function differently for example the estrogen receptor. Both estrogen receptor-α and -β bind to estrogen and share significant homology (95% amino acid identity for DNA-binding domain and 55% amino acid identity for ligand-binding domain). However, estrogen receptor-β functions as a dominant negative molecule in cell proliferation whereas estrogen receptor-α functions in promoting cell proliferation. See Gustafsson, J. A.. Eur J Cancer. 2000 Sep;36 Suppl 4:S16.

The specification does not specify the function of the claimed DNA oligomer as recited in instant claims 18, 21 and 22. Clearly, given not only the teachings of Bowie et al., Scott et al., Burgess et al, and Gustafsson but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, the claimed isolated DNA oligomers with limited homology could not be predicted, based on sequence similarity to a human platelet F11 receptor, nor would it be expected to be the same as that of human platelet F11 receptor. Neither the specification nor any art of record teach the claimed DNA oligomers are related to any

specific disease or establish any involvement of the invention in the etiology of any specific disease. In the absence of any correlation between the claimed DNA oligomers with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Thus, in this instant application, Applicant fails to specify or establish the function or utility of an isolated DNA oligomers as recited in instant claims 18, 21 and 22. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed DNA oligomers. For the reasons given above, Applicant has not established either a specific and substantial asserted utility or a well established utility for the current invention.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 21 and 22 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 22, 23 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 18, 22, 23 and 25 as amended are drawn to DNA oligomers capable of hybridizing in full length under high stringency conditions to the full length of a nucleic acid molecule having/consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO:1, nucleotides 16-912 of SEQ ID NO:1 and nucleotides 97-912 of SEQ ID NO:1 wherein the high stringency hybridization conditions are overnight hybridization at about 68°C in 6XSSC and a wash in 6X SSC at room temperature, followed by a wash at 68°C first in 6XSSC and then in 0.6XSSC, wherein the DNA oligomer has a length of 1822 nucleotides when the DNA oligomer hybridizes to SEQ ID NO:1, the DNA oligomer has a length of 897 nucleotides when the DNA oligomer hybridizes to nucleotides 16-912 of SEQ ID NO:1 and the DNA oligomer has a length of 816 nucleotides when the DNA oligomer hybridizes to nucleotides 97-912 of SEQ ID NO:1 and wherein the nucleotide sequence of SEQ ID NO:1 or nucleotides 97-912 of SEQ ID NO:1 encodes an amino acid sequence selected from the group consisting of SEQ ID NO:3 and amino acid residues 28-299 of SEQ ID NO:3.

The instant claims now recite new limitations "the DNA oligomer has a length of 897 nucleotides when the DNA oligomer hybridizes to nucleotides 16-912 of SEQ ID NO:1 and the DNA oligomer has a length of 816 nucleotides when the DNA oligomer hybridizes to nucleotides 97-912 of SEQ ID NO:1", which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Based on Applicant's response, the support for the new limitation can be found at p. 11, lines 6-18, p. 21, line 4 to p. 22, line2 and p. 29, line 29 to p. 30, line 7. However, no such limitations can be found at the cited pages of the instant specification. The specification only discloses

"a DNA molecule encoding human platelet F11 receptor, or a fragment thereof, the DNA molecule having a nucleotide sequence as shown in SEQ ID NO:l, nucleotides 16-912 of SEQ ID NO:l, nucleotides 97-912 of SEQ ID NO:1..." (see p. 29, line 29 to p. 30, line 7 of the specification).

The scope of the new limitations is different from that of the DNA molecules described in the specification. The specification provides no teaching or guidance as to what is encompassed within the new limitation "the DNA oligomer has a length of 897 nucleotides when the DNA oligomer hybridizes to nucleotides 16-912 of SEQ ID NO:1 and the DNA oligomer has a length of 816 nucleotides when the DNA oligomer hybridizes to nucleotides 97-912 of SEQ ID NO:" Accordingly, in the absence of sufficient recitation of the new limitations, the specification does not provide adequate written description to support the new limitation as recited in claims 18, 22, 23 and 25.

Support is not found for the new limitations as disclosed in the original specification and thus the recitations constitute new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Conclusion

10. NO CLAIM IS ALLOWED.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
December 6, 2010

/Chang-Yu Wang/

Examiner, Art Unit 1649